Section: Obstetrics and Gynaecology

Original Research Article

A STUDY ON ISOSORBIDE MONONITRATE VERSUS DINOPROSTONE GEL FOR CERVICAL RIPENING AT TERM MATERNAL AND FETAL OUTCOME

Rajam.J[1], M.Deepthi Vaishnavi[1]

[1]Assistant Professor, Department of Obstetrics and Gynaecology, Tirunelveli Medical college Hospital, Tamilnadu, India

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Corresponding Author:
Dr. Rajam J,
Email: rajammbbs@gmail.com

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Abstract

Background: Cervical ripening is a crucial step in labour induction that facilitates successful vaginal delivery. This study compared the efficacy and safety of Isosorbide Mononitrate (IMN) and Dinoprostone Gel (PGE2) for cervical ripening at term, evaluating maternal and foetal outcomes. **Materials and Methods:** A prospective, randomised comparative study was conducted on 60 pregnant women at term and requiring labour induction at the Department of Obstetrics and Gynecology, Madurai Medical College. Participants were assigned to two groups: Group A (n=30) received 40 mg of intravaginal IMN every 6 hours based on the Bishop score, while Group B (n=30) received 0.5 mg of PGE2 intracervical at similar intervals, with a maximum of three doses. The Bishop score, induction-to-delivery interval, mode of delivery, maternal side effects, and neonatal outcomes were assessed. Statistical analyses included independent t-tests and chi-square tests, with a significance threshold of $p<0.05$. **Result:** The mean Bishop score after 12 hours was significantly higher in the IMN group (5.63 ± 0.51) than in the PGE2 group (4.33 ± 0.57, p=0.002). Vaginal delivery was achieved in all IMN cases, whereas 20% of PGE2 cases required caesarean delivery (p=0.042). The induction-to-delivery interval was longer in the IMN group (20.36 ± 7.34 h) than in the PGE2 group (16.33 ± 6.56 h, $p<0.001$). Maternal hyperstimulation (20%) and NICU admissions (30%) were observed only in the PGE2 group. **Conclusion:** IMN is a safer and more effective alternative to PGE2 for cervical ripening, with a lower risk of maternal hyperstimulation and neonatal complications. However, it is associated with a longer induction-to-delivery interval than the vaginal route.

INTRODUCTION

Human labour is a complex process characterised by the onset of effective uterine contractions, leading to progressive effacement and dilatation of the cervix, resulting in the expulsion of the foetus, placenta, and membranes.[1] Although most patients have a spontaneous onset of labour at term, labour must be induced for several reasons. Induction aims to achieve a successful vaginal delivery with minimal maternal side effects, and the baby should be born in good condition.[2]

Cervical ripening is the softening and thinning of the cervix in preparation for labor, essential for successful vaginal delivery.[3] An unfavourable cervix can lead to prolonged labor and increased interventions, making effective cervical ripening crucial for improving labor outcomes.[4] Methods for cervical ripening include mechanical (e.g., catheters) and pharmacological (e.g., prostaglandins) approaches.[3] Labor induction rates have significantly increased, with approximately 23% of pregnant women in the US undergoing induction in 2009. Effective cervical ripening is crucial for reducing time to delivery and the incidence of failed inductions.[4]

Dinoprostone gel, a prostaglandin E2 (PGE2) formulation, is an effective cervical ripening agent for labour induction. The intracervical application of PGE2 gel significantly shortens the induction-to-delivery intervals and reduces oxytocin requirements.[5] Although PGE2 gel is generally safe and effective, careful patient selection, proper application technique, and subsequent monitoring of both the mother and foetus are crucial to ensure optimal outcomes.[5] Isosorbide mononitrate (IMN), a nitric oxide donor, has shown promise as a cervical ripening agent. When administered vaginally, IMN effectively induces cervical ripening in first-trimester pregnancies and at term.[6] Compared to prostaglandins, IMN demonstrates a more favourable side effect profile, with headache being the most common complaint.[7] Outpatient administration of IMN before labor induction reduces admission-to-

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delivery intervals and reduces the need for prostaglandins.[8]

Despite existing studies, conclusive evidence on the optimal choice for cervical ripening is lacking, particularly in diverse populations. Most research has been conducted in Western settings, with limited data from Indian or regional obstetric populations. Genetic, physiological, and environmental factors that influence labor outcomes require investigation in diverse patient groups.

Aim

To evaluate the efficacy of isosorbide mononitrate versus dinoprostone gel in cervical ripening at term and compare maternal and foetal outcomes.

MATERIALS AND METHODS

This randomised comparative prospective study was conducted on 60 term cases with obstetric indications for induction at the Department of Obstetrics and Gynaecology, Madurai Medical College, Madurai, India, for 6 months. The Institutional Ethics Committee approved this study prior to its initiation.

Inclusion Criteria

The low-risk group included those with GA of 37 weeks or more at delivery, and the high-risk group included those with DM/HTN/IUGR, single gestation, cephalic presentation, reactive foetal heart rate pattern, and obstetric indications for induction, including post-dated pregnancy, preterm PROM, term PROM, hypertensive disorder, preeclampsia, eclampsia, chronic hypertension, oligohydramnios, and RH isoimmunization.

Exclusion Criteria

Patients with cervical dilatation > 3 cm, Bishop score >5, contraindications for induction (including foetal malpresentation, multiple pregnancies, placenta praevia, previous uterine incision, polyhydramnios, pregnancy with APH, known allergy to drugs, and bronchial asthma) were excluded.

Methods: Informed consent was obtained from each participant. Initial evaluation was performed by taking a complete history, general physical examination, and systemic and obstetric examination. Foetal assessment was performed using Cardiotocography and Biophysical profiles. The study subjects were randomly assigned to two groups of 30 cases each. Group 'A' received T Isosorbide mononitrate 40 mg intravaginally repeated every 6th hour according to the Bishop score. Group 'B' received Dinoprostone Gel 0.5 mg intracervically repeated every 6th hour according to the Bishop score, with a maximum of three doses.

Study Group

Participants in the study group received Isosorbide Mononitrate (40 mg) administered in the posterior fornix. The Bishop score was assessed at 6, 12, and 24 h. If the Bishop score remained <6 at 6 and 12 h, a second and third dose was administered, respectively. Foetal heart rate was monitored every 30 min, and vital signs were recorded every 2 h.

The timing of the first and second doses and the time of delivery were recorded to determine the induction-to-delivery interval. No further doses were administered if the participant spontaneously went into labour or exhibited signs of foetal distress, such as tachycardia, bradycardia, and moderate to severe decelerations on cardiotocography (CTG) or uterine hyperstimulation.

If the Bishop score improved to >6, amniotomy was performed, followed by augmentation if required. If the Bishop score remained <6 after three doses, induction was classified as a failure, and any adverse effects were documented.

Control Group

Participants in the control group were recruited from the antenatal outpatient department (OPD) at GRH and were assessed based on the inclusion criteria. The Bishop score was recorded, and if it was <6, dinoprostone gel (0.5 mg) was administered into the cervical canal. The Bishop score was reassessed at 6, 12, and 24 h. If the score remained <6 at 6 and 12 h, a second and third dose was administered, respectively. Foetal heart rate was monitored every 30 min, and vital signs were recorded every 2 h.

The timing of the first and second doses, along with the time of delivery, was recorded to calculate the induction-to-delivery interval (IDI). No additional doses were administered if the participant spontaneously went into labour or displayed signs of foetal distress, such as tachycardia, bradycardia, moderate to severe decelerations on CTG, or uterine hyperstimulation.

If the Bishop score improved to >6, amniotomy was performed, followed by augmentation if necessary. If the Bishop score remained <6 after three doses, induction was considered a failure, and any adverse effects were documented. Additionally, laboratory tests, including haemoglobin (Hb) levels, platelet count, random blood sugar (RBS), blood urea, serum creatinine, and urine albumin levels, were recorded.

Statistical Analysis: Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to analyse demographic, obstetric, and clinical characteristics. Independent t-tests were used to compare continuous variables (maternal age, gestational age, Bishop score, and induction-to-delivery interval) between the IMN and PGE2 groups. Chi-square or Fisher's exact tests were used for categorical variables (parity, mode of delivery, maternal hyperstimulation, NICU admissions, and Apgar scores). Statistical significance was set at $p < 0.05$.

RESULTS

The mean age was similar in both groups (24.87 in the PGE2 group and 24.13 in the IMN group), and the p-value of 0.375 was not significant. Primigravida was 53.33% in the PGE2 group and 56.67% in the IMN group. Multigravida was 46.67% in the PGE2 group and 43.33% in the IMN group, and the p-value of 0.924 was not significant. In the PGE2 group, 16

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patients were <40 weeks of gestational age, and in the IMN group, 15 patients were <40 weeks of gestational age [Table 1].

Table 1: Demographic And obstetric data.

Category	Parameter	PGE 2 Group (Control) n (%)	IMN Group (Case) n (%)	P-value
Age	<24	10 (33.33%)	16 (53.33%)	0.375
	24-27	14 (46.67%)	7 (23.33%)	
	>27	6 (20%)	7 (23.33%)	
	Mean Age	24.87 ± 3.026	24.13 ± 3.319	
Obstetric code	Primi	16 (53.33%)	17 (56.67%)	0.924
	Multi	14 (46.67%)	13 (43.33%)	
Gestational age	<40	16 (53.33%)	15 (50%)	0.545
	>40	14 (46.67%)	15 (50%)	
	Mean GA SD	39.067 ± 1.23	39.233 ± 0.845	

The mean Bishop score after 12 h was 4.33 ± 0.57 in the PGE2 group and 5.63 ± 0.51 in the study group [Table 2].

Table 2: Bishop score distribution

BISHOP Score	PGE 2 Group (Control)				IMN Group (Case)			
	0 h	6 h	12 h	24 h	0 h	6 h	12 h	24 h
2	1	-	-	-	-	-	-	-
3	26	2	-	-	20	-	-	-
4	3	2	2	-	10	11	-	-
5	-	10	1	-	-	14	4	-
6	-	14	-	-	-	5	7	-
Nil	-	2	27	30	-	19	-	30
Mean SD	3.067 ± 0.365	5.286 ± 0.897	4.333 ± 0.577		3.333 ± 0.479	4.8 ± 0.714	5.636 ± 0.505	
P value	0.019	0.026	0.002					

The number of oligohydramnios cases was eight in the PGE2 group and nine in the IMN group, respectively. The number of postdated cases was 11 in the PGE2 group and 15 in the IMN group. The number of PROM cases was 11 in the PGE2 group and six in the IMN group.

LSCS was more in the PGE2 group (6 cases) but in the IMN group, all cases were delivered by labour natural. The mean induction delivery duration was higher in the IMN group (20.36 h) than in the PGE2 group (16.3 h), with a significant p-value of <0.001 [Table 3].

Table 3: Induction And labor characteristics

Category	Parameter	PGE 2 Group (Control) n (%)	IMN Group (Case) n (%)	P-value
Indication for Induction	Oligohydramnios	8 (26.67%)	9 (30%)	0.007
	Post-dated	11 (36.67%)	15 (50%)	
	Prom	11 (36.67%)	6 (20%)	
	Mean	687.897 ± 275.72	990.0 ± 366.715	
Mode of Delivery	LN	24 (80%)	30 (100%)	0.042
	LSCS	6 (20%)	0	
Induction Delivery Interval	<10 hours	18 (60%)	5 (16.67%)	<0.001
	>10 hours	12 (40%)	25 (83.33%)	
	Mean ± SD	16.33 ± 6.56	20.36 ± 7.34	

In the PGE2 group, six cases had maternal hyperstimulation, whereas none of the cases in the IMN group had maternal hyperstimulation. In the PGE2 group, nine patients required NICU admission, whereas none of the patients in the IMN group required NICU admission [Table 4].

Table 4: Maternal and neonatal outcomes

Category	Parameter	PGE 2 Group (Control) n (%)	IMN Group (Case) n (%)	P-Value
Maternal Hyperstimulation	Yes	6 (20%)	0	-
	No	24 (80%)	30 (100%)	
NICU Admission	Yes	9 (30%)	0	0.002
	No	21 (70%)	30 (100%)	
APGAR Score	5/10 (1 min)	1	0	-
	5/10 (5 min)	0	0	
	6/10 (1 min)	3	1	
	6/10 (5 min)	1	0	
	7/10 (1 min)	24	28	
	7/10 (5 min)	25	5	
	8/10 (1 min)	2	1	
	8/10 (5 min)	4	25	

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DISCUSSION

In our study, the mean age was similar in both groups (24.87 years in the PGE2 group and 24.13 years in the study group). Primigravida was 53.33% in the PGE2 group and 56.67% in the IMN group. Multigravida was 46.67% in the PGE2 group and 43.33% in the IMN group. The parity index was comparable between the two groups. A randomised controlled trial by Malathi and Kanchanamalai reported the age of the majority of participants was between the range of 20-24 years.[9] A randomized controlled trial by Waheed et al. reported a mean age of 27.62 ± 3.909 ranging from 21 to 34 years and the study included only primigravida women.[10]

In our study, the mean Bishop score after 12 h was 4.33+0.57 in the PGE2 group and 5.63 +0.51 in the study group. A randomised controlled trial by Malathi and Kanchanamalai reported the range of gestational age as 37-42 weeks.9 A randomized controlled trial by Pallavi et al. reported median score after 12 hours was lower in the Isosorbide mononitrate group.[11] A study by Agarwal et al. reported the changes in Bishop score between the groups as PGE2: 3.87 ± 1.46, IMN: 3.20 ± 1.61 (p=0.002).[12]

In our study, the mean gestation was 40 weeks and 3 days which was comparable. A randomized controlled trial by Pallavi et al. reported the mean gestation was 40 weeks + 1 d.[11] A study by Agarwal et al. reported the mean gestational age as 37 weeks.[12] The study by Osman et al. reported the mean gestation was 40 weeks 6 days.[13]

In our study, the mean induction delivery was 20.36 h. A randomized controlled trial by Waheed et al. reported the frequency of caesarean section was 12.2% in the Prostaglandin E2 group while 0% in the Isosorbide mononitrate, with no difference.[10] A randomized controlled trial by Pallavi et al. reported the mean induction delivery duration was 25.2 hours.[11] The study by Osman et al. reported the mean induction delivery was 39.7 hrs in the PRIM study.[13]

In our study, five patients in the IMN group were delivered after a single dose of tablet Isosorbide mononitrate, 20 patients were delivered after two doses, and the remaining five patients required three doses for delivery. A randomized controlled trial by Pallavi et al. reported Vaginal delivery occurred in 100% of cases.[11] The study by Osman et al. reported, 36% of cases had vaginal delivery.[13]

In our study, Apgar score < 7 at one minute was only seen in one case (3.3%), and NICU admission was 0% in six cases with maternal hyperstimulation and tachysystole in the PGE2 group, whereas in our study group, there was no maternal hyperstimulation and tachysystole. A randomised controlled trial by Malathi and Kanchanamalai reported NICU admissions and APGAR scores were not significantly different between groups.[9] A randomized controlled trial by Pallavi et al. reported the percentage of babies with Apgar <7 for one minute and NICU admission was 0%.[11] A study by Agarwal et al. reported the Apgar ≤ 3 at 5 minutes only in the high-risk group.[12] The study by Osman et al. reported the percentage of babies with Apgar <7 was 11.7% and NICU admission was 6.6%.[13]

Our study highlights the comparative effectiveness of IMN and dinoprostone gel for cervical ripening at term. Both agents facilitated cervical ripening; however, IMN showed a favourable safety profile with fewer maternal hyperstimulation and neonatal complications despite a prolonged induction-to-delivery interval. Studies by Guha et al. and Habib et al. show IMN results in fewer cases of uterine tachysystole and hyperstimulation.[14,15] Soliman's study confirms IMN's safety profile compared to misoprostol and combination therapy.[16]

CONCLUSION

Isosorbide mononitrate is cheaper and more effective than prostaglandin E2 for cervical ripening at term in normal pregnancy. IMN does not cause uterine hyperstimulation or maternal tachysystole. IMN does not cause non-reassuring fetal heart rate patterns IMN does not cause neonatal side effects. The induction delivery interval was prolonged in the IMN group (mean 20.36 hours), and the study group's mean delivery interval was 16.32 hours.

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